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Does the Identity of the Third-Party Payer Matter for Prescribing Doctors?

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Abstract

TNF-alpha inhibitors represent one of the most important areas of biopharmaceuticals by sales, with three blockbusters accounting for 8 per cent of total pharmaceutical sale in Norway. Novelty of the paper is to examine, with the use of a unique natural policy experiment in Norway, to what extent the price responsiveness of prescription choices is affected when the identity of the third-party payer changes. The three dominating drugs in this market, Enbrel, Remicade, and Humira, are substitutes, but have had different and varying funding schemes - hospitals and the national insurance plan. A stochastic structural model for the three drugs, covering demand and price setting, is estimated in a joint maximum likelihood approach. We find that doctors are more responsive when the costs are covered by the hospitals compared to when costs are covered by national insurance.

Keywords: pharmaceuticals, discrete choice model, funding-schemes.

JEL-Code: C35, D43, I18, L11.

1. Introduction

The agency problem faced by insurance companies and governments, and its consequences for health care financing has been subjected to extensive theoretical and empirical research (McGuire, 2000). The moral hazard problem in health care arises due to third-party funding and doctors' superior information about diagnosis and preferred treatment choices. In an insurance-based health care system there are at least two candidates for being the third-party payer. When prescribing a drug on behalf of an insured patient, the cost may be covered by traditional insurance plans – private or public – on a fee-for-service basis - or by the hospital with which the doctor and patient are affiliated. In Norway the main sources of health care financing are national (public) insurance plans and hospital budgets, financed with grants from the government.

The agency problem differs between a global hospital funding scheme and a fee-for-service approach adopted by traditional insurance plans. Treatment costs covered by the national insurance plan do not represent a direct cost for the doctor and the hospital. To the extent that treatment costs still affect the choice of drug under a pure national insurance plan funding can be explained by doctors' understanding and adherence to national guidelines for cost-effective treatment choices. However, when treatment costs are covered by the hospital, the opportunity costs becomes more "tangible" to the doctors. Increased treatment costs on one patient reduce available resources for other activities at the affiliated hospital. For this reason, treatment choices may be under a tighter control or monitoring when costs are covered by the local hospital instead of a national, and tax funded, insurance plan.

With use of a unique natural policy experiment in Norway, we are able to investigate to what extent the price responsiveness of prescription choices is affected when the identity of the third-party payer changes. Our case in point is the Norwegian market for Tumor Necrosis Factor (TNF) alpha inhibitors (Note[i]).

When the market for TNF-inhibitors opened in Norway in 2000, the first entrant Enbrel was fully covered by the obligatory national insurance plan. The treatment with Enbrel is initiated by the hospital doctor, but the cost was automatically covered by the national insurance plan. The second entrant Remicade did not obtain the same type of

coverage. Instead, the doctor's affiliated hospital was held responsible for the treatment cost. Importantly, the hospital's budget did not include earmarked grants for these patients. Cost of treatment with Remicade, therefore, was covered by the hospital's general grant from the government, and as such competed with other expenses within the hospital. This sharp asymmetry in funding scheme reflects a quality attribute of the two drugs. Enbrel is administrated by the patients themselves (pump injections), while Remicade requires several hours infusion at hospitals. In fall 2002 the government modified the plan for Remicade by reducing the hospital's copayment from 100 to 20 per cent. The remaining 20 per cent was still covered the hospital's general grant, and not by the activity-based scheme (DRG). Enbrel maintained its full insurance plan coverage. The third entrant Humira is also administrated by pump injections by patients, and received the same funding plan as Enbrel when the drug entered in January 2003.

The important policy change exploited in our study took place in 2006. Then the asymmetry of financing between Enbrel, Humira, and Remicade was removed by returning the entire funding responsibility to the hospitals for all three drugs. All drug costs related of treatment with TNF-alpha inhibitors had to be covered by the hospital's general grant (Note[ii]). The policy change was based on a claim that the previous scheme created, from the government's perspectives, an unintentional demand response, not related to differences in drug prices (Note[iii]). By transferring the funding responsibility for all three drugs to the hospitals, the government aimed at a more neutral scheme with respect to doctor's treatment choices.

By creating large and exogenous variations in hospital and insurance plan treatment costs, these funding switches becomes the crucial source of identification in our empirical model. To investigate how the different funding plans affected price responses among doctors, we have specified a discrete choice model in which the doctor's choice of TNF-alpha inhibitors depends on the prices and the funding schemes. The discrete choice model results in three market share equations (the aggregates of multinomial logit probabilities). To account for the possibility that quality aspects, including side effects of the drugs, are priced out in the market we have modeled the price setting of the producers, derived from a non-cooperative Nash-equilibrium. The markets share equations and the price setting equations are estimated jointly on aggregate monthly data. The results show that doctors' choice of TNF-alpha inhibitor is responsive to price differences, and that this price response becomes stronger when hospitals cover the costs.

The reminder of the paper is organized as follows. In Section 2 we relate our paper to the existing literature. Section 3 presents the econometric model and Section 4 presents the data. Section 5 gives the results and Section 6 concludes.

2. Related Literature

Our research relates to two strands of the health economics literature. One is the literature on pharmaceutical demand and price elasticities. The other is the literature studying the effect of reimbursement schemes on spending. However, these two areas of research are interlinked since many of the studies of price responses in pharmaceutical demand exploit variations in reimbursement schemes and patient charges.

Ellison, Cockburn, Griliches, and Hausman (1997) estimate a demand model for a class of anti-infective drugs called cephalosporins. Their data contains four different chemical substances, and three of these substances experienced significant generic entry in the sample period. In the case of substitution between different substances (therapeutic substitution), they find evidence of low (and often insignificant) price responses in demand. Price responses are stronger when the choice is between brand-name and generics (generic substitution). One of the drugs comes out with a significant own-price elasticity of −0.3. Cephalosporin drugs differ from our TNF-alpha inhibitors by having a relatively low level of hospital consumption.

Berndt, Pindyck, and Azoulay (2003) estimate a demand model for a growing market with competing brand-names available. They use data for H2-antagonist antiulcer, and their data starts at the entry of the first patent (Tagament). Similar to our study, therefore, they investigate the pharmaceutical demand in a market with several competing brand-name (patented) drugs. They develop a rich model that includes a dynamic component of diffusion. Their market share model allows the drug choice to depend on prices, in addition to marketing. Doctors' are found to respond to prices, but similar to the findings of Ellison et al. (1997), price responses appear to be relatively low. They find own-price elasticities in the range of about −0.3 and −0.6.

There is a larger literature studying the demand responses to changes in co-payment by patients. A seminal contribution was made by Leibowitz, Manning, and Newhouse (1985), who used data from the Rand Health Insurance experiment to study the relationship between the degree of cost sharing with patients and prescription drug utilization. They found that patients with a more generous insurance scheme buy more prescription drugs. Another early contribution, using monthly time-series from the National Health Service (NHS) in England, is O'Brien (1989). He found co-payment elasticities in the range of about −0.3 and −0.6. A more recent contribution along this line of research is made by Contoyannis, Hurley, Grootendorst, Jung, and Tamblyn (2005). Using micro data (individual patients) from Quebec, they estimate the elasticity of expenditure for prescription drugs with respect to patients' marginal prices (cost sharing).

These were found to be relatively low - in the interval −0.12 to −0.16.

Iizuka (2007) is a recent contribution to the literature on agency problems in the prescription drug market. In the Japanese market, doctors make profit from selling prescribed drugs. Using data with both prices and doctors' own mark-up, he estimates a nested logit demand model for the hypertension market, including 40 brands in 5 different therapeutic classes. Iizuka finds that prescription decisions are influenced by the size of mark-up, but that doctors care more about patient welfare than their own profit. Hence, if the retail price of a brand increases, the doctor becomes less likely to prescribe that drug. Other papers studying the importance of doctor and prices in prescription choices are Coscelli (2000) and Lundin (2000). The latter study relates to our analysis by showing that doctors' responses to prices are influenced by the funding source. In Lundin's analysis the two funding sources are the patients themselves or the insurance provider. The main contribution of Lundin is to show how the level of patients' co-payment influences doctors choices (between generics and brand-name). He finds that doctors' are more responsive to patients' co-payment than the cost of the insurance provider.

Hellerstein (1998) provides evidence of the importance of insurance plans for the agency problem in prescription choices. She finds that doctors with a higher fraction HMO-patients (Health Maintenance Organization) relative to patients who are enrolled in traditional insurance plans, more often prescribe generics instead of the brand-name drug. Because her data did not contain prices, she is not able to study price responsiveness.

3. Econometric Models

The decision-making unit on the demand side is the physician, who acts as the patient's agent (Arrow, 1963). Therefore, decision-making-units (DMU) are here represented by physician-patient couples, $i=1,..\ N_t$.

The model is derived from a random utility model (see Train, 2009 for an overview of such models) in which DMUs chooses among the available drugs, $j=1,..,J$, to maximize utility.

The number of drugs is three. To this end they are numbered: Enbrel no1, Humira no2 and Remicade no3. The number of periods (months) is 62. Our data set include more months. However, capacity problems for the manufacture of Enbrel created a lot of noise in the market in the years 2001-2002. To avoid this noise in the data we decided to exclude these months in our analysis.

Utility for the decision-making unit is given by

$$U_{ijt} = -v_{jt}p_{jt} + a_{jt} + \varepsilon_{ijt};\ i=1,2,,,N_t;\quad j=1,2,3;\ \ t=1,2,,,62 \tag{1}$$

where a_{it} is an indicator of perceived treatment quality of drug j at time t. This is a common quality-indicator that applies to all patients that can benefit from TNF-alpha therapy. Like in Berry et al (1995) we will assume that a_{it} depends on observed as well as unobserved attributes, which will be specified below. The unobserved part may reflect quality attributes of the three drugs that could be priced out in the market and hence the unobserved parts may correlate with prices. This creates estimation problems that will be addressed below. p_{jt} is the price variable associated with drug j at time t and v_{jt} are coefficients that capture the impact of the costs of treatment on utility. We have specified the price part of the utility function so that a negative impact of price on utility requires v_{jt} to be positive. The random variable ε_{ijt} is iid extreme value.

The costs of treatment with TNF-alpha inhibitors are covered by a third-party. There are two third-party payers. One is the National Insurance Plan (NIS) (termed "I"), and the other is the hospital with which the prescribing doctor is affiliated (termed "H"). The funding split between the insurance plan and the hospital varies over time and across drugs: At a given time *t* the drug costs are fully paid by the hospital, fully covered by the insurance plan, or split between the two with 80 percent covered by insurance and 20 percent by hospitals.

Thus, v_{jt} is given by:

$$v_{jt} = \alpha_{Ijt}\beta_I + \alpha_{Hjt}\beta_H;\ j=1,2,3 \tag{2}$$

Where

$$\begin{aligned} \alpha_{Ijt} &= \{1,\ \ 0.8,\ \ 0\} \\ \alpha_{Hjt} &= \{0,\ \ 0.2,\ \ 1\} \end{aligned} \tag{3}$$

The β-s are coefficients and represent the doctor's responses to drug costs under the different funding plans.

When the market for TNF-apha inhibitors opened in 2000, Enbrel was fully covered by NIS (i.e. α_{I1t}=1), whereas Remicade was covered by the hospitals (α_{H3t} =1). In the fall 2002, the funding of Remicade changed. Hospitals had to pay 20 per cent, whereas NIS paid the remaining 80 per cent (α_{I3t} =0.8, α_{H3t} =0.2). When entering in 2003, Humira was given the same funding plan as Enbrel, i.e. fully coverage by NIS (α_{I2t} =1). In June 2006, the government then gave the full funding responsibility to the hospitals for all three drugs (α_{Hjt} =1 for all j.).

Because hospitals face budget constraints, the hospital's opportunity costs of drug treatment are strictly positive.

Reduced treatment costs may benefit other activities and patients at the same hospital. With coverage by the national insurance plan, the direct opportunity cost of the hospital will be zero. Choosing a drug that is fully paid by the insurance plan has no impact on the resources available for other activities at the hospital. However, doctors have guidelines that instruct them to be cost consciousness in their choices of treatment. Therefore, we expect doctors to be price responsive also in the case of insurance plan coverage. But, in the case where the hospital pays the treatment costs, we expect doctors to become more concerned about these costs. This might be due to the personal incentives of doctors' to economize on costs in order to be able to spend extra resources on other patients, or just due to the fact that the hospital management has stronger incentives to monitor the individual doctor's treatment choices when these involve hospitals own budgets.

Our hypothesis thus is that (remember that positive coefficients imply a negative impact of price on utility):

$$H_0: \quad b_H = b_I$$
$$H_I: \quad 0 < b_I < b_H$$

Because ε_{ijt} is assumed to be independently, identically extreme value distributed across individuals and products, the probability that the decision-making unit *i* will choose drug *j* at time *t* is given by the following multinomial logit probabilities:

$$\varphi_{ijt} = \varphi_{jt} = \Pr\left(U_{ijt} = \underset{k=1,2,3}{\text{Max}}\, U_{ikt}\right) = \frac{\exp(-v_{jt}p_{jt} + a_{jt})}{\sum_{k=1}^{3}\exp(-v_{kt}p_{kt} + a_{kt})}; \quad j=1,2,3 \tag{4}$$

We choose Enbrel to be the reference product, here denoted product 1, and if we assume there is no outside good whose utility can be normalized to zero, these probabilities can be written (Note [iv]):

$$\varphi_{jt} = \frac{\exp(a_{jt} - a_{1t} - (v_{jt}p_{jt} - v_{1t}p_{1t}))}{1 + \sum_{k=2}^{3}\exp(a_{kt} - a_{1t} - (v_{kt}p_{kt} - v_{1t}p_{1t}))} \quad j=2,3; \quad t=1.2....62$$
$$\varphi_{1t} = \frac{1}{1 + \sum_{k=2}^{3}\exp(a_{kt} - a_{1t} - (v_{kt}p_{kt} - v_{1t}p_{1t}))} \tag{5}$$

The observed parallel to the average of agents' probabilities is the market share of the product, m_{jt}. Because we only exploit aggregate data, our observed variables will be the market shares.

The coefficient a_{jt} is assumed to depend on three parts: a deterministic drug-specific constant, α_j, a time trend, $\beta_j t$, and a stochastic variable e_{jt}. The deterministic drug-specific constants reflects some unobserved drug-specific elements, while the two others may reflect some factors related to doctors' perception of quality which may change over time and some of this is also unobserved.

This gives us the following log-odd ratios:

$$\log\frac{m_{2t}}{m_{1t}} = \alpha_2 - (v_{2t}p_{2t} - v_{1t}p_{1t}) + \beta_2 t + e_{2t} \tag{6}$$

$$\log\frac{m_{3t}}{m_{1t}} = \alpha_3 - (v_{3t}p_{2t} - v_{1t}p_{1t}) + \beta_3 t + e_{3t} \tag{7}$$

As mentioned in the introduction there are reasons to expect that quality aspects captured by the error terms, e_{2t} and e_{3t}, can correlate with prices. The empirical results, given in Section 5, confirm this expectation. We deal with this problem by modeling a simultaneous demand and price setting model.

We assume that each drug provider sets the price on its drug so that expected profit is maximized, given the market share equations for the three drugs and the prices set by the other two providers. In this approach we also account for a possible correlation between the error terms in the model. This means that in addition to control for quality being priced out in the market, we also control for a variety of unobserved heterogeneity.

The market share equations for all three drugs can be written as:

$$m_{1t} = \frac{1}{1 + \sum_{j=2}^{3}\exp(\alpha_j - (v_{jt}p_{jt} - v_{1t}p_{1t}) + \beta_j t + e_{jt})} \tag{8}$$

$$m_{2t} = \frac{\exp(\alpha_2 - (v_{2t}p_{2t} - v_{1t}p_{1t}) + \beta_2 t + e_{2t})}{1 + \sum_{j=2}^{3}\exp(\alpha_j - (v_{jt}p_{jt} - v_{1t}p_{1t}) + \beta_j t + e_{jt})} \tag{9}$$

$$m_{3t} = \frac{\exp(\alpha_3 - (v_{3t}p_{3t} - v_{1t}p_{1t}) + \beta_3 t + e_{3t})}{1 + \sum_{j=2}^{3} \exp(\alpha_j - (v_{jt}p_{jt} - v_{1t}p_{1t}) + \beta_j t + e_{jt})} \quad (10)$$

Note that we have:

$$\frac{\partial m_{jt}}{\partial p_{jt}} = -v_{jt} m_{jt}(1 - m_{jt}); \quad j=1,2,3 \quad (11)$$

Expected profits of the seller of drugs are:

$$\pi_{jt} = (p_{jt} - C_{jt}) N_t m_{jt} \quad (12)$$

Here C_{jt} are unobserved unit costs. In estimating the model we will assume that $C_{jt}=c_{jt}+\eta_{jt}$, where $c_{jt}=c_j$ will be estimated below and η_{jt} is an unobserved part of the unit cost and/or unobserved factors in the profit maximization process. N_t is the number of potential customers.

Maximizing expected profit with respect to price yield the following first order conditions:

$$p_{jt} = C_{jt} + \frac{1}{v_{jt}(1 - m_{jt})}; \quad j=1,2,3. \quad (13)$$

The econometric model we estimate thus is an equilibrium model. Eqs. (14) and (15) are the demand side of the market, while equations (16)-(18) give the supply side in terms of pricing equations. Our conjecture is that β_I and β_H are positive. If the latter is the highest one, funding through hospital budget yields more price-responsiveness than through social insurance. Furthermore we expect that correlation across the random terms is such that if there is negative price shock in the market for the cheapest and least efficient drug, Remicade, there will be a negative price shock in the market for Enbrel. The negative price shock in the Remicade market will cet.par. increase the market share for Remicade. Due to the monopolistic competition in the market the producer of Enbrel will respond by cutting its price. But a negative correlation in the unobserved parts of market shares of Remicade and Enbrel will cet.par. raise the price of Enbrel and thus counteract this price cut. Thus the higher quality drug Enbrel may preserve its market share even with a smaller price cut than what the observed part of monopolistic competition predicts. To our knowledge we are the first to model econometrically this mechanism.

$$\log \frac{m_{2t}}{m_{1t}} = \alpha_2 - (v_{2t}p_{2t} - v_{1t}p_{1t}) + \beta_2 t + e_{2t} \quad (14)$$

$$\log \frac{m_{3t}}{m_{1t}} = \alpha_3 - (v_{3t}p_{3t} - v_{1t}p_{1t}) + \beta_3 t + e_{3t} \quad (15)$$

$$p_{1t} = c_1 + \frac{1}{v_{1t}(1 - m_{1t})} + \eta_{1t} \quad (16)$$

$$p_{2t} = c_2 + \frac{1}{v_{2t}(1 - m_{2t})} + \eta_{2t} \quad (17)$$

$$p_{3t} = c_3 + \frac{1}{v_{3t}(1 - m_{3t})} + \eta_{3t} \quad (18)$$

where

$$v_{jt} = \alpha_{Ijt}\beta_I + \alpha_{Hjt}\beta_H; \quad j=1,2,3$$

We will allow for correlation across the random variables. The correlation structure is the following:

$$e_{2t} = \rho_2 \eta_{2t} + \mu_{2t} \quad (19)$$

$$e_{3t} = \rho_3 \eta_{3t} + \mu_{3t} \quad (20)$$

$$\eta_{1t} = \rho_{12}\eta_{2t} + \rho_{13}\eta_{3t} + \mu_{1t} \quad (21)$$

where

μ_{it} is normally distributed $N(0,\sigma_i)$

From (17) and (19) we get:

$$e_{2t} = \rho_2 \left(p_{2t} - c_2 - \frac{1}{v_{2t}(1-m_{2t})} \right) + \mu_{2t} \quad (22)$$

From (18) and (20) we get

$$\varepsilon_{3t} = \rho_3 \left(p_{3t} - c_3 - \frac{1}{v_{3t}(1-m_{3t})} \right) + \mu_{3t} \tag{23}$$

And finally we have

$$\eta_{1t} = \rho_{12} \left(p_{2t} - c_2 - \frac{1}{v_{2t}(1-m_{2t})} \right) + \rho_{13} \left(p_{3t} - c_3 - \frac{1}{v_{3t}(1-m_{3t})} \right) + \mu_{1t} \tag{24}$$

The endogenous (stochastic) variables in our model are the market shares and the prices. In order to derive the distribution of these variables, given the distribution of the error terms in the previous equations, we have to obtain the probability law of the observed random variables, $\{m_{1t}, m_{2t}, m_{3t}, p_{1t}, p_{2t}, p_{3t}\}$. Basically this means that we multiply into the likelihood of the sample the numerical value of the Jacobian of transformation (see Haavelmo (1944), p 87). The Jacobian determinant gives the derivatives of the error terms in each of the 6 equations above with respect to the 6 observed random variables present in the equations. If the Jacobian determinant explicitly depends on the unknown coefficients that we estimate, then it matters for the estimation to include the absolute value of the Jacobian determinant. This is the case here. The likelihood that we maximize with respect to the unknown coefficients is given in equation (25). In estimating the model the three c-s are assumed to be constant over time.

As mentioned above our method of estimation is maximum likelihood. The estimates we obtained are those which maximises L in equation (25). The second derivatives are used to yield standard errors.

$$\begin{aligned} L = \prod_{t=1}^{62} & \frac{1}{\sigma_2} f \left(\frac{\log(m_{2t}) - \log(m_{1t}) - \alpha_2 + (v_{2t}p_{2t} - v_{1t}p_{1t}) - \beta_2 t - \rho_2 \left(p_{2t} - c_{2t} - \frac{1}{v_{2t}(1-m_{2t})} \right)}{\sigma_2} \right) \\ & \times \frac{1}{\sigma_3} f \left(\frac{\log(m_{3t}) - \log(m_{1t}) - \alpha_3 + (v_{3t}p_{3t} - v_{1t}p_{1t}) - \beta_3 t - \rho_3 \left(p_{3t} - c_{3t} - \frac{1}{v_{3t}(1-m_{3t})} \right)}{\sigma_3} \right) \\ & \times \frac{1}{\sigma_1} f \left(\frac{p_{1t} - c_{1t} - \frac{1}{v_{1t}(1-m_{1t})} - \rho_{12} \left(p_{2t} - c_{2t} - \frac{1}{v_{2t}(1-m_{2t})} \right) - \rho_{13} \left(p_{3t} - c_{3t} - \frac{1}{v_{3t}(1-m_{3t})} \right)}{\sigma_1} \right) \\ & \times \frac{1}{\sigma_{\eta 2}} f \left(\frac{p_{2t} - c_{2t} - \frac{1}{v_{2t}(1-m_{2t})}}{\sigma_{\eta 2}} \right) \\ & \times \frac{1}{\sigma_{\eta 3}} f \left(\frac{p_{3t} - c_{3t} - \frac{1}{v_{3t}(1-m_{3t})}}{\sigma_{\eta 3}} \right) \\ & \times |J_t| \end{aligned} \tag{25}$$

where f(.) is the unit normal probability density and $|J_t|$ is the absolute value of the determinant of the Jacobian given by

$$= \begin{vmatrix} \frac{m_{1t}+m_{2t}}{m_{1t}m_{2t}} & \frac{1}{m_{1t}} & -v_{1t} & v_{2t} & 0 \\ \frac{1}{m_{1t}} & \frac{m_{1t}+m_{3t}}{m_{1t}m_{3t}} & -v_{1t} & 0 & v_{3t} \\ -\frac{1}{v_{1t}(1-m_{1t})^2} & -\frac{1}{v_{1t}(1-m_{1t})^2} & 1 & 0 & 0 \\ -\frac{1}{v_{2t}(1-m_{2t})^2} & 0 & 0 & 1 & 0 \\ 0 & -\frac{1}{v_{3t}(1-m_{3t})^2} & 0 & 0 & 1 \end{vmatrix} \tag{26}$$

4. Data

There are three biotechnological drugs acting as *t*umor *n*ecroses *f*actor (TNF) alpha inhibitor in the treatment of rheumatoid arthritis (RA). Enbrel (etanercept), is a recombinant protein of human origin. It was approved by the Food

and Drug Administration (FDA) in 1998 for the reduction of signs and symptoms of moderate to severe RA, and in Europe by European Medicin Agency (EMEA) in 1999. It is administered twice a week by subcutaneous injection. At the time of introduction, it was indicated for use by patients who had an inadequate response to one of the other disease-modifying anti-rheumatic drugs (DMARD) (Moreland, Baumgartner, & Schiff, 1997). In combination with Rheumatrex (methotrexate) clinical trials proved that the addition of etanercept to methotrexate therapy resulted in rapid and sustained improvement (Weinblatt, Kremer, Bankhurst, & Bulpitt, 1999). Enbrel gained approval also for the treatment of juvenile RA and psoriatic arthritis, and further studies demonstrated its effectiveness as compared with methotrexate in patients with early active RA (Bathon, Martin, & Fleischmann, 2000), making it a first-line treatment for RA and a leading brand within the new class of DMARDs. Enbrel was developed by Immunex, a biotechnology company that in 2001 was acquired by Amgen.

The second TNF-based RA product on the market is Remicade (infliximab), a chimeric (human and mouse) monoclonal antibody that proved to be safe and effective with persistently active RA not responding to methotrexate therapy (Lipsky, Van Der Heijde, St Clair, & Furst, 2000). It is marketed by Centocor together with Schering Plough and the Japanese company Mitsubishi Tanabe Pharma. In Europe EMEA granted marketing authorization in March 2000. It is administered every four to eight weeks via an intravenous infusion that may take several hours to complete and requires qualified personnel monitoring of adverse reactions. This is considered as a disadvantage in comparison with Enbrel. Nevertheless, Remicade progressively increased its sales gaining high market shares. Price of Remicade is lower than Enbrel.

The third TNF alpha inhibitor in the market is Humira (adalimumab), a fully human monoclonal antibody approved by FDA in December 2002 and by EMEA in September 2003, and marketed by Abbott in the form of subcutaneous injection every two weeks, setting the drug price in parity with Enbrel. Its attracting dosing profile was considered a key success factor, but relatively short after its launch, the growth of sales slowed and it seemed not to threaten significantly the market position of its two competitors.

Market penetration in terms of sales value of these three drugs has been highly successful in Norway. Sale of Enbrel, Remicade and Humira accounted for 8 per cent of total pharmaceutical sale in Norway in 2008 (Note[v]).

The dataset consists of monthly wholesale value and quantity sold, expressed in defined daily doses (DDD), for each of the three drugs Enbrel, Remicade and Humira (Note[vi]). The data set covers the months from January 2000 to March 2008, indicated as running from t=1 to t=99 in Figures 1 and 2. The price per DDD is constructed from combining the value and quantity information. Figure 1 shows the monthly wholesale value of sale.

The market opened early 2000, with the entry of both Enbrel and Remicade. Enbrel had a far stronger growth during the first year, and became soon the leading drug. In 2001-2002 Enbrel experienced problems of supplying the global market. Worldwide capacity shortage forced the producer to reduce the sale of Enbrel in Norway. This explains the drastic reduction in sale value for Enbrel, and its volatility shown in Figure 1.

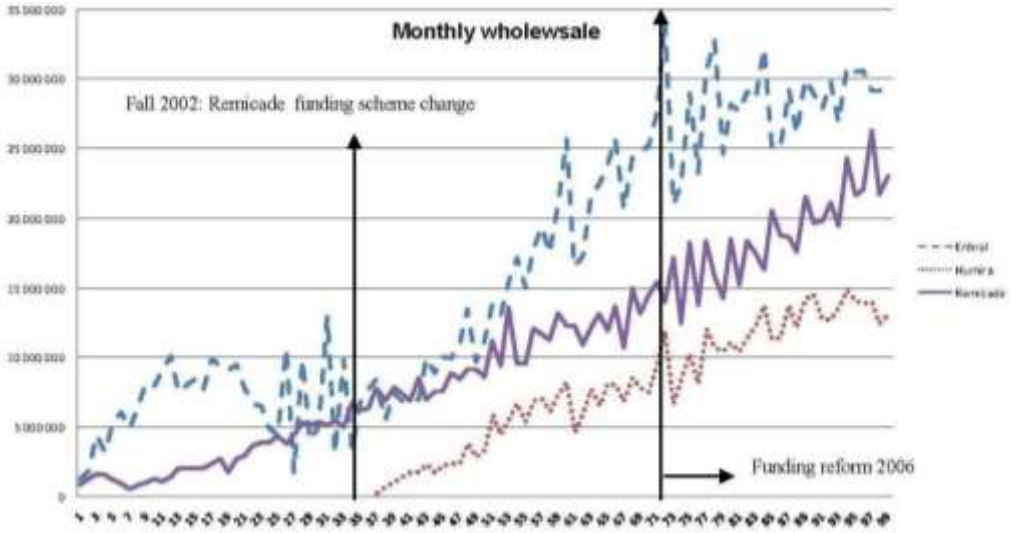

Figure 1. Monthly wholesale value of sale; 1000 NOK. As of Sept 2013 1 Euro=NOK 7.90

In the fall 2003, the third drug, Humira, entered. Although Humira experienced a steady growth in the fast growing market, it never succeeded in capturing a larger market share. Figure 2 shows the development of market shares.

Figure 2. Market shares for the three drugs (DDD).

Within the first year, Enbrel reached a market share of 80 percent. The market share dropped rapidly, most triggered by the abovementioned shortage of production capacity. Since Remicade was the only alternative TNF-inhibitor in this period, it experiences an equivalent rise in its market share. Humira reached a market share close to 9 percent after a few months.

The price of Enbrel has always been very high relative to Remicade. Except for the first couple of months, the wholesale price of Enbrel per DDD stayed between 350 and 400 NOK until late fall 2001. Then the price dropped to a level closer to 300 NOK per DDD. Remicade started out with a price of 200 per NOK, but came down to a level between 160 and 170 NOK per DDD after a few months. Humira entered with a price much higher than the price of Enbrel. Although Humira has kept its position as the price leader, the price gap (compared with Enbrel) has been narrowed during the sample period. Figure 3 shows the development of wholesale prices. As mentioned in the introduction. Enbrel, Humira and Remicade had different and varying funding schemes over time.

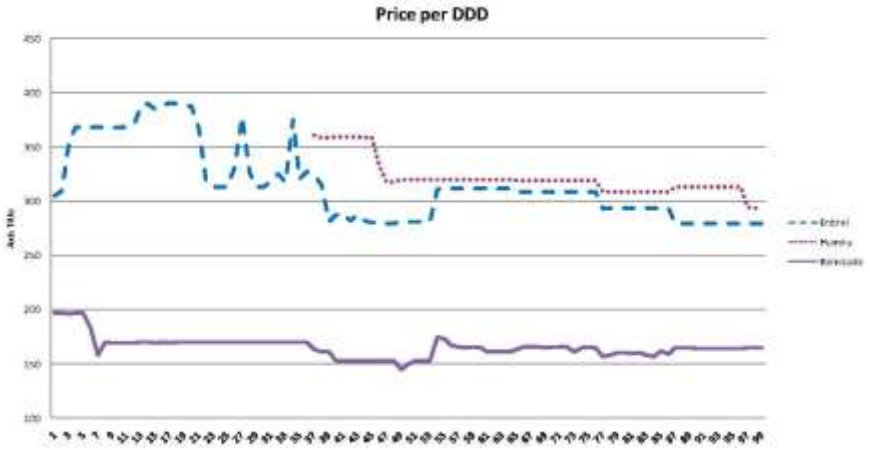

Figure 3. Wholesale price, NOK per DDD.

We have chosen to restrict the sample period in our empirical analysis to t=38-99 for several reasons. First, there are reasons to expect demand behavior – and in particular price responses – to be different in the early stage of a new pharmaceutical market compared with the more maturated market. In the early stage, doctors are unfamiliar with the particular technology of treatment (TNF-alpha inhibitors) – both its efficiency and its possible side-effects. In a more mature market, doctors have gained experience with the drug, and will be better able to make treatment choices for the individual patients (see See Berndt et al. (2003)). Gaining experience with TNF-inhibitors, the doctors will be better able to take treatment costs into account when choosing between the available alternatives. Second, capacity shortage for the manufacture of Enbrel during the first years distorts demand. As seen in this Section, Enbrel experienced a sharp decline in sale 2001-2002 that was due to a global capacity problem of the manufacture. After a period of decline, sale and market shares were very unstable, until problems were resolved some months before the entry of Humira.

Summary statistics for the sample used in estimating our models are provided in Table 1.

5. Results

First, we show the estimates of the coefficients $\{\alpha_2,\alpha_3,\beta_1,\beta_H,\beta_2,\beta_3\}$ when only the demand model is used (Table 2).

The point estimates imply that $\beta_I < \beta_H$, but the 95 per cent confidence intervals overlap: lower limit for β_I is 0.8581 and upper limit is 4.4450, and for β_H the lower limit is 2.2627 and the upper limit is 6.7633. The problem with this estimation is that the error terms in the market share equations may be correlated with the prices. There are several reasons for this and one is that prices are set by the drug providers so that unobserved quality aspects are priced out. When regressing the predicted squared residuals against prices we get significant results which clearly indicate that homoscedasticity is rejected.

Berry et al (1995) recommend that the constants in the equations above should vary across observations and hence represent the unobserved quality attributes that may be correlated with price. Next, these coefficients should be regressed against prices, or calibrated. The problem in our case with that approach is the high number of constants; here equal to the number of observations. We have therefore chosen to model demand and the price setting of drugs and estimate market shares and price setting equations simultaneously. The estimates are given in Table 3.

Table 1. Summary statistics (62 obs.)

Variable	Mean	Std. Dev.	Min	Max
Enbrel:				
DDD	73413.7300	28228.5300	17534.0000	111829.0000
market share	0.3860	0.0379	0.2802	0.4764
price	0.2942	0.0136	0.2794	0.3146
sales	21572.0700	8128.4650	5515.4780	34216.2800
α_{H1}	0.3548	0.4824	0.0000	1.0000
α_{I1}	0.6452	0.4824	0.0000	1.0000
Humira:				
DDD	26143.3400	13833.7300	2014.0000	47531.0000
market share	0.1278	0.0362	0.0322	0.1720
price	0.3206	0.0163	0.2935	0.3591
sales	8206.7740	4197.8050	722.3141	14838.1300
α_{H2}	0.3548	0.4824	0.0000	1.0000
α_{I2}	0.6452	0.4824	0.0000	1.0000
Remicade:				
DDD	88812.0800	30046.7300	43019.0000	159655.0000
market share	0.4862	0.0651	0.3639	0.6876
price	0.1608	0.0056	0.1446	0.1743
sales	14341.7000	5026.1530	6901.8260	26308.0300
α_{H3}	0.4839	0.3859	0.2000	1.0000
α_{I3}	0.5161	0.3859	0.0000	0.8000

Table 2. The demand model

Coefficients	Estimates	t-values
β_I	2.652	2.90
β_H	4.513	3.93
β_2 (Humira)	0.014	11.30
β_3 (Remicade	-0.011	-4.77
α_2 (Humira)	-2.066	-20.49
α_3 (Remicade)	0.587	3.03
Number of observations	62	
R^2 (Humira)	0.7476	
R^2 (Remicade)	0.2351	

Now, the predicted values of the squared residuals in the market share equations do not vary significantly with prices and thus homoscedasticity is **not** rejected. The 95 per cent confidence intervals for the β_I and β_H do overlap just a little:lower limit for β_I is 11.018 and the upper limit is 12.2785, and for β_H the lower limit is 12.1640 and the upper limit is 13.8808. A 90 per cent interval does not overlap: lower limit for β_I is 11.1276 and the upper limit is 12.1624, and for β_H the lower limit is 12.3214 and the upper limit is 13.7266. Based on this model there are some clear evidences that doctors are more responsive when the hospitals cover the expenses compared to when national insurance is taking up the bill.

In Figure 4 we show the observed development over time of the market shares as well as the prediction based on the demand model only and on the model where demand and pricing is estimated jointly. We observe that the latter model better predicts the observed development, including the market shares after the reform. In Appendix B we give the numbers of observed and predicted market shares over time month by month.

Table 3. Joint estimates of market shares and price setting

Coefficents	Estimates	t-values
β_I	11.645	37.02
β_H	13.022	30.57
β_2 (Humira)	1.161	6.46
β_3 (Remicade)	-0.032	-0.08
α_2 (Humira)	-1.635	-13.05
α_3 (Remicade)	-1.340	-4.705
c_1	0.159	36.76
c_2	0.226	66.36
c_3	~0	~0
σ_1	0.010	11.01
σ_2	0.187	11.01
σ_3	0.176	4.02
$\sigma_{\eta 2}$	0.017	10.93
$\sigma_{\eta 3}$	0.032	10.56
ρ_2	3.718	1.93
ρ_3	-4.901	-1.69
ρ_{12}	-0.177	-1.36
ρ_{13}	-0.078	-1.025
Log Likelihood	1055.700	
No of observations	62	

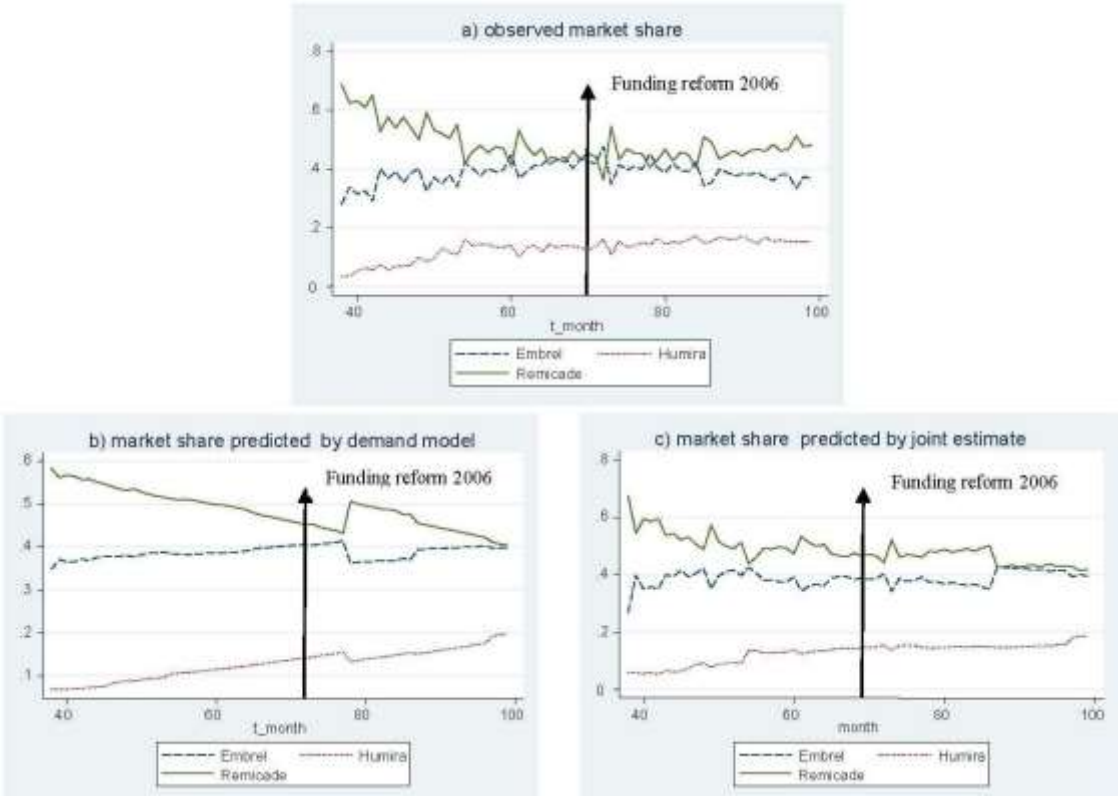

Figure 4. Market share a) observed, b) predicted by demand model, c) predicted by joint estimate, from month 38 (February 2003) to month 99 (March 2008)

In Appendix A we report the model and the results when the model is extended to deal with autocorrelation in all error terms. The estimates of the autoregressive coefficients are all positive, between 0 and 1, and clearly significant. More importantly, the estimates of β_I and β_H do not change much.

When autocorrelation is accounted for the trend effects in market shares (β_2 and β_3) both are insignificant. The drug specific constants (α_2 and α_3) are estimated to be negative (relative to Enbrel). Now both are significant and the numerical values become higher, in particular for Remicade. These results indicate that given the price, Enbrel is a favored drug in particular compared to Remicade. This accord with the fact that Enbrel yields a more efficient treatment and requires less time use for the patient, and with less side effects, than Remicade.

All unit costs are now significant and almost of the same magnitude as in Table 3, in particular for Enbrel and Humira. When accounting for autocorrelation, there is no clear impact on the estimates of the variances of the error terms. However, the correlation between the unobserved factors in the market share of Remicade and its price setting is now estimated to be significantly negative. Also the correlation between the unobserved factors in the price setting of Enbrel and Remicade is estimated to be significantly negative. The first means that if there is negative shock in the price of Remicade, then its market share increases, cet.par. The latter estimate implies that a negative price shock for Remicade has a positive impact on the prices of Enbrel. However, it should be noticed that due to the observed part in the price setting equation for Enbrel a lower price of Remicade implies also a negative price response for Enbrel. This is due to the monopolistic competition among the three producers. The negative correlation between the unobserved factors in the price setting of Enbrel and Remicade modifies this price response and is obviously due to unobserved quality characteristic across the two drugs. The better quality of Enbrel makes it possible to reduce the price less as a response to a negative shift in the price of Remicade. This lesser response is here captured by the probabilistic structure of the price setting part in the model.

To further compare the results of the three models we show mean own-price elasticities. These elasticities are the elasticities of expected demand with respect to the prices p_{jt}. The elasticities are calculated by applying the following expression:

$$E_{jt} = \frac{p_{jt}}{m_{jt}} \frac{\partial \hat{m}_{jt}}{\partial p_{jt}} = -v_{jt} p_{jt} (1-\hat{m}_{jt}); \quad j=1,2,3 \tag{27}$$

Table 4. Mean price elasticities

I

	The market share model	Demand and price setting approach	As the previous one, with autocorr.
Enbrel	-0.59	-2.19	-2.34
Humira	-0.92	-3.39	-3.63
Remicade	-0.29	-1.02	-1.09

We cleary see that when unobserved quality and hence, statistical endogeneity, is controlled for, the numerical value of the price elasticities increases. To account for autocorrelation has a negligible impact on the elasticities.

The reason why the elasticities are numerical higher when demand and pricing are estimated jointly is that unobserved quality effects absorbed in the random parts of the demand model, and correlated with price, are priced out in the market. The joint model with correlation across random terms in the demand equations as well as in the pricing equations, account for these market aspects. A more well-known example from another market is that if the demand for wine is estimated, lumping all types of wine together, one get low numerical values of demand elasticities. The reason is that the model treats high quality wine with a high price the same way as low quality wine with a low price. Again unobserved quality of wine, priced out in the market, correlates with price in the demand model, and hence an estimate of the demand model only will give biased results.

In Figure 5 we report the elasticities month by month based on the joint model.

	Hospital funding	Insurance funding
Enbrel		
from 2000 to 2006	$\alpha_{EH} = 0$	$\alpha_{E} = 1$
after 2006	$\alpha_{EH} = 1$	$\alpha_{E} = 0$
Humira		
from 2000 to 2003	not in the market	
from 2003 to 2006	$\alpha_{HH} = 0$	$\alpha_{H} = 1$
after 2006	$\alpha_{HH} = 1$	$\alpha_{H} = 0$
Remicade		
from 2000 to 2002	$\alpha_{RH} = 1$	$\alpha_{R} = 8$
from 2002 to 2006	$\alpha_{RH} = 0.2$	$\alpha_{R} = 0.8$
after 2006	$\alpha_{RH} = 1$	$\alpha_{R} = 0$

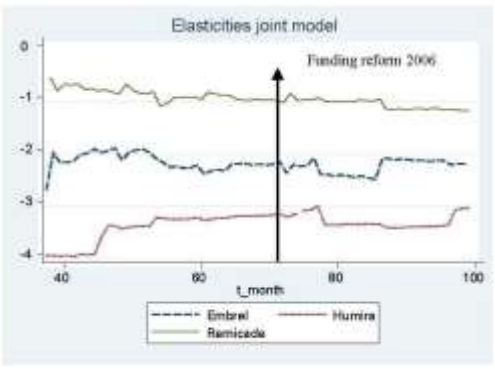

Figure 5. Funding scheme and elasticities based on the joint estimates of market shares and price setting.

6. Conclusions

We have employed a discrete choice model in which the doctor's choice among TNF-alpha inhibitors depends on the prices. Price response is allowed to vary with the identity of the third-party payer, national insurance and hospitals. The estimate of the resulting market share model indicates that homoscedasticity is rejected, which may be due to neglected unobserved quality aspects of the drugs which are priced out in the market. The traditional way of dealing with this problem is to instrument the prices. We have used another approach. We have modeled the market equilibrium for the three drugs. Prices are determined in a non-cooperative Nash – equilibrium. We include correlation between market share equations and price setting equations. We also account for autocorrelation by estimating an AR1 model. The equilibrium model is estimated in a joint maximum likelihood approach.

We find that doctors are significantly more responsive when the costs are covered by the hospitals compared to when costs are covered by national, public insurance. Moreover, the numerical values of the own-price elasticities increase substantially when a market share model is replaced by a market equilibrium model.

An interesting result emerges due to the estimated correlation structure of the model. The correlation between the unobserved factors in the market share of Remicade (the less expensive and less efficient treatment) and its price setting is estimated to be significantly negative. This implies that if there is negative shock in the price of Remicade, then its market share increases, cet.par.. Due to the observed part of the price setting in the monopolistic competition model the producer of Enbrel (and also of Humira) respond by cutting prices. However, the correlation between the unobserved factors in the price-setting of Enbrel (the more expensive and more efficient treatment) and of Remicade is estimated to be significantly negative. This negative correlation between the unobserved factors in the price setting of Enbrel and Remicade therefore modifies the price response due to the observed part of price-setting and is obviously due to unobserved quality characteristc across the two drugs. The better quality of Enbrel makes it possible to reduce the price **less** as a response to a negative shift in the price of Remicade. This lesser response is here captured by the probabilistic structure of the price-setting part of the model. To our knowledge we are the first to model and estimate this outcome of an equilibrium model.

The policy implication of our finding is that the funding schemes of expensive drugs matter with respect to the costs to the society of using drugs with more or less similar treatment effects but with marked price differentials. In Norway a reform was introduced in 2006 transferring the funding responsibility for all drugs from social insurance to hospitals. This made the prescribing doctors more cost conscious and implied a more neutral scheme with respect to treatment choices. In many of the members of EU, with Italy as an exception, the funding scheme is social insurance. Our results indicate that to put the funding inside the hospital budgets may lower the costs of using TNF-alpha inhibitors.

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Appendix A. The market model extended to deal with autocorrelation.

To simplify notation let $Y_{2t}=\frac{\log m_{2t}}{\log m_{1t}}, Y_{3t}=\frac{\log m_{3t}}{\log m_{1t}}$, and let r_j, j=2,3,4,5,6 be the coefficients that capture the possible correlation over time between the error terms in the equations (14)-(18).

For instance $e_{2t}=r_2\, e_{2t-1}+ e^*_{2t}$, where * indicate the new error terms after assuming a first order autoregressive scheme. The equivalent to equations (14)-(18) is then

$$Y_{2t}=r_2Y_{2t-1}-(v_{2t}p_{2t}-v_{1t}p_{1t})+r_2(v_{2t-1}p_{2t-1}-v_{1t-1}p_{1t-1})+\beta_2(1-r_2)t+r_2\beta_2+(1-r_2)\alpha_2+e^*_{2t} \quad (14^*)$$

$$Y_{3t}=r_3Y_{3t-1}-(v_{3t}p_{3t}-v_{1t}p_{1t})+r_3(v_{3t-1}p_{3t-1}-v_{1t-1}p_{1t-1})+\beta_3(1-r_3)t+r_3\beta_3+(1-r_3)\alpha_3+e^*_{3t} \quad (15^*)$$

$$p_{1t}=r_4p_{1t-1}+(1-r_4)c_1+\frac{1}{v_{1t}(1-m_{1t})}-r_4\frac{1}{v_{1t-1}(1-m_{1t-1})}+\eta^*_{1t} \quad (16^*)$$

$$p_{2t}=r_5p_{2t-1}+(1-r_5)c_2+\frac{1}{v_{2t}(1-m_{2t})}-r_5\frac{1}{v_{2t-1}(1-m_{2t-1})}+\eta^*_{2t} \quad (17^*)$$

$$p_{3t}=r_6p_{3t-1}+(1-r_6)c_3+\frac{1}{v_{3t}(1-m_{3t})}-r_5\frac{1}{v_{3t-1}(1-m_{3t-1})}+\eta^*_{3t} \quad (18^*)$$

where as before $v_{jt}=\alpha_{Ijt}\beta_I+\alpha_{Hjt}\beta_H$; i=1,2,3

The likelihood now becomes

$$L=\prod_{t=1}^{62}\frac{1}{\sigma_2}f\left(\frac{Y_{2t}-r_2Y_{2t-1}+(v_{2t}p_{2t}-v_{1t}p_{1t})-r_2(v_{2t-1}p_{2t-1}-v_{1t-1}p_{1t-1})-\beta_2(1-r_2)t-r_2\beta_2-(1-r_2)\alpha_2-\right.$$
$$\left.-\rho_2\left(p_{2t}-r_5p_{2t-1}-(1-r_5)c_2-\frac{1}{v_{2t}(1-m_{2t})}+r_5\frac{1}{v_{2t-1}(1-m_{2t-1})}\right)}{\sigma_2}\right)$$
$$\times\frac{1}{\sigma_3}f\left(\frac{Y_{3t}-r_3Y_{3t-1}+(v_{3t}p_{3t}-v_{1t}p_{1t})-r_3(v_{3t-1}p_{3t-1}-v_{1t-1}p_{1t-1})-\beta_3(1-r_3)t-r_3\beta_3-(1-r_3)\alpha_3-\right.$$
$$\left.-\rho_3\left(p_{3t}-r_6p_{3t-1}-(1-r_6)c_3-\frac{1}{v_{3t}(1-m_{3t})}+r_5\frac{1}{v_{3t-1}(1-m_{3t-1})}\right)}{\sigma_3}\right)$$
$$\times\frac{1}{\sigma_1}f\left(\frac{p_{1t}-r_4p_{1t-1}-(1-r_4)c_1-\frac{1}{v_{1t}(1-m_{1t})}+r_4\frac{1}{v_{1t-1}(1-m_{1t-1})}-\rho_{12}\left(p_{2t}-r_5p_{2t-1}-(1-r_5)c_2-\frac{1}{v_{2t}(1-m_{2t})}+r_5\frac{1}{v_{2t-1}(1-m_{2t-1})}\right)-\right.$$
$$\left.-\rho_{13}\left(p_{3t}-r_6p_{3t-1}-(1-r_6)c_3-\frac{1}{v_{3t}(1-m_{3t})}+r_5\frac{1}{v_{3t-1}(1-m_{3t-1})}\right)}{\sigma_1}\right)$$
$$\times\frac{1}{\sigma_{\eta2}}f\left(\frac{p_{2t}-r_5p_{2t-1}-(1-r_5)c_2-\frac{1}{v_{2t}(1-m_{2t})}+r_5\frac{1}{v_{2t-1}(1-m_{2t-1})}}{\sigma_{\eta2}}\right)$$
$$\times\frac{1}{\sigma_{\eta3}}f\left(\frac{p_{3t}-r_6p_{3t-1}-(1-r_6)c_3-\frac{1}{v_{3t}(1-m_{3t})}+r_5\frac{1}{v_{3t-1}(1-m_{3t-1})}}{\sigma_{\eta3}}\right)$$
$$\times|J_t|$$

where f(.) is the unit normal probability density and $|J_t|$ is the absolute value of the same determinant of the Jacobian as before. The estimates are given in Table A.1.

Table A.1. Joint estimates of market shares and price setting, accounting for autocorrelation.

Coefficents	Estimates	t-values
β_I	12.842	7.75
β_H	13.368	7.86
β_2 (Humira)	0.556	1.68
β_3 (Remicade)	0.836	0.95
α_2 (Humira)	-2.400	-2.51
α_3 (Remicade)	-8.868	-0.91
c_1	0.167	10.27
c_2	0.223	17.47
c_3	0.111	2.69
σ_1	0.007	10.74
σ_2	0.129	9.51
σ_3	0.104	8.03
$\sigma_{\eta2}$	0.005	10.51
$\sigma_{\eta3}$	0.018	6.83
ρ_2	3.649	0.88
ρ_3	-10.040	-7.94
ρ_{12}	-0.048	-0.25
ρ_{13}	-0.299	-5.26
r_2	0.691	7.60
r_3	0.890	17.18
r_4	0.664	6.36
r_5	0.878	24.34
r_6	0.662	2.87
Log Likelihood	1225.700	
No of observations	62	

Appendix B. Market share observed and predicted by different models

Table B.1. Monthly market share: observed, predicted by the demand model, and predicted by joint model

Year	month number	month	observed			predicted:demand model			predicted: joint model		
			Embrel	Humira	Remicade	Embrel	Humira	Remicade	Embrel	Humira	Remicade
2003	38	February	0.33	0.00	0.67	0.35	0.07	0.58	0.27	0.06	0.68
	39	March	0.35	0.00	0.65	0.37	0.07	0.56	0.40	0.06	0.54
	40	April	0.36	0.00	0.64	0.36	0.07	0.57	0.35	0.05	0.59
	41	May	0.40	0.00	0.60	0.36	0.07	0.57	0.36	0.06	0.59
	42	June	0.39	0.00	0.61	0.37	0.07	0.56	0.35	0.05	0.60
	43	July	0.35	0.00	0.65	0.37	0.07	0.56	0.40	0.07	0.54
	44	August	0.41	0.00	0.59	0.38	0.07	0.55	0.39	0.06	0.54
	45	September	0.35	0.05	0.60	0.38	0.07	0.55	0.42	0.06	0.52
	46	October	0.32	0.11	0.57	0.38	0.08	0.54	0.39	0.07	0.53
	47	November	0.33	0.12	0.55	0.38	0.09	0.54	0.41	0.09	0.51
	48	December	0.37	0.14	0.49	0.38	0.09	0.53	0.42	0.09	0.49
2004	49	January	0.36	0.16	0.48	0.38	0.09	0.54	0.35	0.08	0.57
	50	February	0.39	0.15	0.46	0.38	0.09	0.53	0.40	0.09	0.52
	51	March	0.38	0.16	0.46	0.39	0.09	0.52	0.41	0.09	0.50
	52	April	0.32	0.16	0.52	0.39	0.09	0.52	0.42	0.09	0.49
	53	May	0.36	0.15	0.49	0.39	0.10	0.52	0.40	0.09	0.51
	54	June	0.40	0.15	0.45	0.38	0.10	0.51	0.43	0.14	0.44
	55	July	0.38	0.20	0.42	0.38	0.11	0.51	0.41	0.13	0.46
	56	August	0.38	0.17	0.45	0.38	0.11	0.51	0.38	0.13	0.49
	57	September	0.40	0.20	0.40	0.38	0.11	0.51	0.38	0.13	0.49
	58	October	0.41	0.16	0.43	0.38	0.11	0.51	0.38	0.13	0.50
	59	November	0.42	0.15	0.43	0.39	0.11	0.50	0.38	0.13	0.49
	60	December	0.44	0.16	0.40	0.39	0.11	0.50	0.39	0.14	0.47
2005	61	January	0.43	0.15	0.43	0.39	0.12	0.50	0.34	0.12	0.53
	62	February	0.45	0.16	0.40	0.39	0.12	0.49	0.36	0.13	0.51
	63	March	0.40	0.17	0.43	0.39	0.12	0.49	0.37	0.13	0.50
	64	April	0.39	0.16	0.45	0.39	0.12	0.49	0.36	0.13	0.51
	65	May	0.45	0.17	0.38	0.40	0.12	0.48	0.39	0.14	0.47
	66	June	0.41	0.17	0.42	0.40	0.13	0.47	0.39	0.14	0.47
	67	July	0.42	0.19	0.39	0.40	0.13	0.47	0.39	0.14	0.46
	68	August	0.43	0.17	0.40	0.40	0.13	0.47	0.38	0.14	0.47
	69	September	0.41	0.19	0.40	0.40	0.13	0.46	0.39	0.15	0.47
	70	October	0.42	0.21	0.37	0.40	0.14	0.46	0.38	0.15	0.47
	71	November	0.44	0.21	0.35	0.40	0.14	0.46	0.39	0.15	0.46
	72	December	0.41	0.21	0.39	0.41	0.14	0.45	0.40	0.15	0.44
2006	73	January	0.39	0.22	0.38	0.40	0.14	0.45	0.34	0.14	0.52
	74	February	0.40	0.22	0.37	0.41	0.15	0.45	0.39	0.15	0.46
	75	March	0.40	0.22	0.38	0.41	0.15	0.44	0.38	0.15	0.47
	76	April	0.40	0.24	0.36	0.41	0.15	0.44	0.38	0.15	0.47
	77	May	0.41	0.23	0.36	0.41	0.15	0.43	0.39	0.15	0.46
	78	June	0.38	0.24	0.38	0.36	0.13	0.51	0.37	0.14	0.48
	79	July	0.38	0.26	0.36	0.36	0.14	0.50	0.37	0.15	0.48
	80	August	0.39	0.27	0.34	0.37	0.14	0.50	0.37	0.14	0.49
	81	September	0.38	0.27	0.35	0.37	0.14	0.49	0.37	0.15	0.48
	82	October	0.39	0.26	0.35	0.37	0.14	0.49	0.37	0.15	0.48
	83	November	0.37	0.27	0.35	0.37	0.14	0.49	0.36	0.15	0.49
	84	December	0.40	0.28	0.32	0.37	0.15	0.48	0.37	0.15	0.48
2007	85	January	0.36	0.27	0.37	0.37	0.15	0.48	0.36	0.15	0.49
	86	February	0.37	0.29	0.34	0.37	0.15	0.48	0.35	0.15	0.50
	87	March	0.37	0.27	0.36	0.39	0.15	0.46	0.43	0.15	0.43
	88	April	0.36	0.27	0.36	0.39	0.15	0.45	0.43	0.15	0.43
	89	May	0.38	0.28	0.34	0.40	0.16	0.45	0.42	0.15	0.43
	90	June	0.37	0.29	0.35	0.40	0.16	0.44	0.42	0.15	0.43
	91	July	0.36	0.30	0.34	0.40	0.16	0.44	0.42	0.15	0.43

	92	August	0.37	0.29	0.34	0.40	0.16	0.44	0.42	0.15	0.43
	93	September	0.36	0.29	0.35	0.40	0.17	0.43	0.42	0.15	0.43
	94	October	0.37	0.32	0.32	0.40	0.17	0.43	0.41	0.15	0.44
	95	November	0.36	0.31	0.33	0.40	0.17	0.43	0.42	0.16	0.43
	96	December	0.36	0.33	0.31	0.40	0.18	0.42	0.41	0.16	0.43
2008	97	January	0.33	0.30	0.37	0.40	0.19	0.41	0.39	0.18	0.43
	98	February	0.35	0.32	0.33	0.40	0.20	0.41	0.40	0.19	0.42
	99	March	0.35	0.32	0.33	0.40	0.20	0.40	0.40	0.19	0.42

Notes

Note[i]. To date TNF-alpha inhibitors represent the most important way to treat arthritis and other autoimmune diseases (Feldmann & Maini, 2003).

Note[ii]. With the change of the funding scheme in 2006, Remicade was given a fee-for-service to compensate for the need for in-hospital infusion of the drug. Importantly, although Enbrel and Humira is administered by the patient and delivered by local pharmacies, the prescrpition choices are always made by doctors affiliated with the hospitals.

Note[iii]. According to the government's budget proposal presented to the Parliament (Stortinget) September 30, 2005. The general grant to hospitals was increased to compensate for the increased drug costs related to these drugs.

Note[iv]. Unfortunately, we are not able to construct an outside option to treatment with one of the three therapies. This would require a record of all patients with these diagnoses – including those without medical treatment. Our model, therefore, assumes that variations in prices covered by hospitals or the insurance schemes only affects the allocation of patients on different therapies (drugs), and not the total number of patients treated.

Note[v]. Norwegian Association of Pharmaceutical Manufacturers. Facts and Figures (2009).

Note[vi]. The data set is provided by Farmastat, a company owned by Norwegian Association of Pharmaceutical Manufacturers.